POSSIBILITY OF REDUCING THE TOXIC ACTION OF CARBON DIOXIDE ON THE LIVING ORGANISM

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Despite numerous investigations of the effect of changes in the percentage content of CO_2 on the animal organism, very little study has so far been given to the prolonged action of small concentrations of CO_2 on the body. Data in the literature [6, 10, 11] show that even a small rise in the CO_2 percentage in the inspired air may have an unfavorable influence on the state of the organism, reducing the ability to work and the resistance to various factors (physical exertion, respiration under increased pressure, overloading, etc.). /305

The range of compensation which is possible by the body relative to the gaseous components of atmospheric air (CO_2, O_2) is very limited. Sensitivity of the body is particularly high to CO_2, oxygen taking second place. So far as nitrogen is concerned, although it is present in the atmosphere in high concentration its complete replacement by helium evidently has no appreciable effect on the body [2].

The smaller the percentage of a biologically active gas in the inspired air, the more sensitive the body therefore is to an increase in its percentage. In fact, in order to produce hyper- or hypoventilation, it is only necessary to change the concentration of CO_2 in the alveolar air by $\pm 0.5\%$. Meanwhile, an increase or decrease of several percent in the oxygen concentration has no appreciable effect on changes in respiration. Consequently, the body is much more sensitive to changes in the concentration of carbon dioxide than of oxygen.

At the same time, however, the body is many times more resistant to an increase in the CO_2 concentration in the inspired air than in the oxygen concentration. If, for example, the partial pressure of CO_2 in the inspired air is increased by 20 times compared with that in the ordinary atmosphere (from 0.23 to 4.56 mm Hg), only a change in respiration is produced, whereas an analogous increase in the partial pressure would cause death of the organism from hyperoxemia (an increase of pO_2 from 159.5 to 3192 mm Hg, i.e., to 4.2 atm. pure oxygen).

Any change in the gaseous composition of the surrounding atmosphere, accompanied by a change in the composition of the alveolar air, may disturb the constancy of composition of the internal milieu of the organism. The inevitable consequence of this is the occurrence of compensatory reactions by various systems of the body, and especially of increased respiratory function and cardiovascular activity. /306

If compensation is well developed, the organism may begin to function on a new level. However, in some cases such compensation costs the body very dearly, especially if the action of the gaseous environment of modified composition continues for a long time. If, therefore, the composition of the gaseous environment is changed for a long time, reliance cannot be placed entirely on the adaptive, defensive reactions of the body itself. It may receive important aid under these conditions from the creation of optimal proportions between the gaseous components of the atmosphere, at which the unfavorable action of an increase in one of them will be masked by the positive effect of the action of another gaseous component. Such an effect may be anticipated because of the well-known biological antagonism between CO_2 and oxygen and of the mechanisms of compensatory reactions of the body during exposure to changed concentrations of these gases.

In this connection it is pertinent to recall investigations which demonstrated the beneficial effect of addition of CO_2 to hypoxemic mixtures on the body [3,7], the potentiation of the narcotic action of high CO_2 concentrations by a decrease in the oxygen concentration in the inspired mixture to 12-15% [4], and the shortening of the recovery period after prolonged CO_2 poisoning by administration of pure oxygen [5].

These investigations show that if the organism is exposed to modified conditions of its gaseous environment, its state will depend on the ratio between the oxygen and CO_2 concentrations. They also confirm P. M. Al'bitskiy's view [1] that definite antagonism between oxygen and carbon dioxide exists in the living organism.

It may be supposed that the basis of antagonism between oxygen and CO_2 is the difference between the action of these gases on the state of the metabolic processes, which are inhibited by carbon dioxide and stimulated by oxygen within a definite range of their concentrations.

For the sake of these considerations we decided to conduct an investigation in order to find ways of preventing the toxic action of CO_2 on the body.

In our investigations during previous years we found that if animals are kept for 5-6 h or for many days in a gaseous environment with 3-5% CO_2, this is followed by a long period of inhibition of activity of the central nervous system. If, on the other hand, the gas mixture is enriched with oxygen (to 35-40%), the period of this aftereffect is reduced by half. /307

This suggested that oxygen could be used to limit the unfavorable effects of carbon dioxide on the animal organism.

The most marked unfavorable effect of prolonged exposure to CO_2 was expressed as lowering of the animal's resistance to overloads, to breathing under

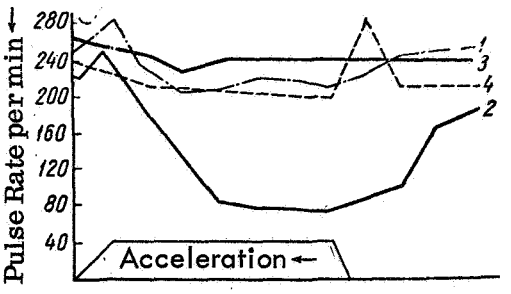

Figure 1. Changes in Heart Rate of Rabbits During the Action of Radial Accelerations Before and After a Stay in a Gaseous Environment with an Increased CO_2 Concentration and with Different Oxygen Concentrations.

1 and 3) in Initial State; 2) After a Stay in 5% CO_2 for 5h; 4) After a Stay in 5% CO_2 and 34% O_2 for 5 h.

increased pressure, and to physical exertion. If the animals were kept for 5 h in 5% CO_2 and a normal oxygen concentration, for instance, in some cases disturbances of cardiac activity developed (disturbances of conduction and excitation of the myocardium, myocardial infraction) during overloads, together with paresis of the hind limbs, prolonged desynchronization of the α-rhythm on the EEG, and so on.

After an increase in the concentration of oxygen in the gaseous mixture to 35%, the ability of the animals to tolerate overloads, as shown by the changes in respiration, pulse, ECG and EEG, was affected relatively little by comparison with what took place before the animals' stay in the gaseous environment. Curves of the changes in the pulse of rabbits subjected to the action of radial accelerations of identical magnitude before and after a stay in a gaseous environment with an increased CO_2 concentration and with different concentrations of oxygen may serve as an example (Fig. 1). They show clearly that both the degree of inhibition of cardiac activity and the time taken for it to recover were much reduced if an increased concentration of oxygen was present.

In an autopsy on animals subjected to the action of accelerations after a stay in a gaseous environment with an increased CO_2 concentration extensive hemorrhages located mainly along the course of the ribs were very often found. If the gas mixture contained an increased percentage of oxygen, the hemorrhages in the lungs were small and petechial. Many emphysematous areas were found. Histological analysis (V. B. Barsukovskiy) after exposure to CO_2 and overloading revealed multiple hemorrhages (partial and massive) in the interstitial tissue and also hemorrhages inside the alveoli. /308

In rabbits subjected to overloads after a stay in a gaseous environment with 5% CO_2 and enriched with oxygen, tiny, scattered interstitiah hemorrhages were found. Sometimes collections of erythrocytes were observed in the walls of the alveoli (incrustation). The impression was created that CO_2 makes the vessels more permeable and that an increase in the oxygen concentration in the gaseous medium to some degree prevents the development of these undesirable phenomena. Unfortunately the small number of histomorphological examinations carried out does not allow more definite conclusions to be drawn.

Convincing data concerning the beneficial action of oxygen in relation to the changes caused by CO_2 were obtained in experiments in which high CO_2 concentrations were used. The object of these investigations was to study the character of the course of the "inverse" action of carbon dioxide depending on the partial pressure of oxygen. The pattern of development of the "inverse" action of CO_2 was different in cases when mice were preliminarily kept in a gaseous environment with 40% CO_2 and with a partial pressure of oxygen equal to 160 or 350 mm Hg.

TABLE: Inverse Action of CO_2 in Relation to Partial

Pressure of Oxygen and Preceding Administration of Vitamins to Animals

Series	Experimental conditions	Character of inverse action of CO_2		
		full recovery	incomp. recovery	death
I	Mice taken from gaseous environment with 40% CO_2 and pO_2 = 160 mm Hg . . .	51	26	23
II	Mice taken from gaseous environment with 40% CO_2 and pO_2 = 305 mm Hg . . .	15	71	14
III	Mice taken from gaseous environment with 40% CO_2 and placed in one with pO_2 = 380 mm Hg, ...	39	54	7
IV	Mice (vitaminized) taken from gaseous environment with 40% CO_2 and pO_2 = = 160 mm Hg	68	16	16
V	Mice (vitaminized) taken from gaseous environment with 40% CO_2 and pO_2 = = 305 mm Hg	42	51	7

In the first case, after a stay in carbon dioxide the mice had an attack of well marked clonic spasms lasting the first 1.5 min. They coincided in time with a period of slowing of respiration. Often the attack terminated in spastic respiratory arrest and death of the animal. If, however, the animal did not die, its movements were inhibited for a long time.

When the partial pressure of oxygen in the gaseous mixture was increased to 305 mm Hg, the spasms appeared sooner and the individual spasms were shorter in duration and less severe. The recovery period was considerably longer in duration, but the mortality rate among the animals was greatly reduced (table).

Further analysis of the results showed that among animals receiving vitamins the best results were obtained with those treated with vitamins concerned with synthetic processes in the cells: vitamin B_{12}, folic, pantothenic and p-aminobenzoic acids (N.D. Popov). Their administration sharply reduced the mortality rate among the mice taken from an environment with a high CO_2 concentration.

A factor of considerable importance in increasing the resistance of the body to the action of carbon dioxide is nonspecific acclimatization to various agents: a lowered partial pressure of oxygen and long-acting overloads (Chang Ju-kuo). /309

Experiments showed that adaptation to hypoxia, besides increasing the resistance of the body to this factor, at the same time increases its resistance to changed conditions of the gaseous environment, containing low and high concentrations of CO_2.

Repeated daily exposure of animals to small (up to 1.5 g) overloads for a duration of 60 min for 5 days also increased their resistance to high concentrations of CO_2 in the inspired air.

These investigations thus confirmed once again the existence of highly complex interactions in the body between the biologically active gases oxygen and carbon dioxide; they showed that an increase in the concentration of one gas (oxygen) essentially modifies the manifestation of toxicity of the other. The action of both these gases is evidently directed toward the tissue enzyme systems, the level of whose activity provides optimal conditions for metabolic processes to take place.

This is a matter of great importance for function of those nervous centers on whose activity rests the smooth flow of the chain of compensatory reactions aimed at maintaining equilibrium between the organism and the modified conditions of the gaseous environment. Provision is thus made for increasing the resistance of the organism to unfavorable factors by modifying its reactivity in the required direction. /310

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